REMARKS

The above-identified application has been carefully reviewed in light of the Office Action mailed December 20, 2000. Enclosed is a Request for Extension of Time, and required fee, extending the period for responding to the Office Action to and including April 20, 2001.

Claim 66 has been amended to make clear that the components of the agents are covalently attached.

Attached is a version of claim 66 with markings to show the amendments.

Claims 1 to 65 have been canceled, without prejudice.

New claims 67 to 80 have been added and are directed to embodiments for which patent protection is sought. These new claims are fully supported by the present specification, originally filed.

The pending office action set forth the following requirements and rejections:

Restriction Requirements

The claims in the application were restricted into three groups, as follows:

Group I: claims 1-20, 26-35 and 66

Group II: claims 21-25, 36 and 37

Group III: claims 38-65

The Examiner requested affirmation of the provisional election of Group I.

Applicant hereby affirms the election of claims directed to compositions as found in Group I. The non-elected claims in Group II and III have been canceled without prejudice.

Furthermore, Applicant has canceled claims 1 to 20 and 26 to 35, without prejudice, and has added new claims 67 to 80 for the

purpose of facilitating prosecution. Applicant strongly disagrees with Examiner on the rejections of these claims, for example, for many of the reasons set forth below with regard to the present pending claims. The amendments to claim 66 and the new claims 67 to 80 have not been presented for any reason related to statutory requirements of patentability and/or the claims as a whole have not been narrowed. Hence, the presently pending claims are not subject to the rule set forth in Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki, Co., 56 USPQ 2d 1865 (Fed. Cir. 2000).

Rejections under 35 U.S.C. 112, First Paragraph

Claims 1-10, 12-13, 15-19 and 26-34 have been rejected under 35 U.S.C. 112, first paragraph. The Examiner alleges that the application does not provide enabling disclosure for making or using the invention within the scope of the claims. In particular, the Examiner alleges that the application does not provide sufficient enablement to make or use an agent comprising any transmission compound as a targeting moiety other than substance P.

Claims 1-10, 12-13, 15-19 and 26-34 have been canceled, without prejudice. Therefore, this rejection is moot. However, Applicant disagrees with this rejection and reserves the right to continue prosecution of the canceled claims at a future date.

Contrary to the Examiner's allegation, the specification does include an enabling disclosure with respect to making the various types of transmission compounds. The specification also discloses the use of these compounds. See the present specification, for example, at page 8, line 16 through page 9, line 9; page 16, line 18 through page 17, line 4; page 18, lines 17-20; page 18, lines 21-25; page 22, line 28 through page 23, line 6; page 23, lines 6-20; page 25, lines 6-12; page 28, lines 6-27; page 33, line 11 through page 33, line 22; page 34, line 22 through page 36, line 1; and page 36, lines 3-9.

Rejections under 35 U.S.C. 112, Second Paragraph

Claims 1-20 and 26-35 have been rejected under 35 U.S.C. 112, second paragraph. Claims 1-20 and 26-35 have been canceled, without prejudice, to facilitate prosecution. Therefore, these rejections are moot.

However, applicant disagrees with the Examiner on these rejections and reserves the right to continue prosecution of the canceled claims at a future date.

Claim 66 has been rejected as being indefinite under 35 U.S.C. 112, second paragraph. Applicant traverses this rejection.

As written, claim 66 clearly states that the agent is attached as follows: (proteolytic domain)-(translocation domain)-(substance P). Claim 66 has also been amended to clarify that the various components are covalently attached.

In view of the above, applicant submits that claim 66, and new claims 67 to 80 satisfy the requirements of 35 U.S.C. 112, second paragraph.

Rejections Under 35 U.S.C. 102(b) and (e)

Claims 1-9, 12, 18-19 and 26-35 have been rejected under 35 U.S.C. 102(b) and 102(e) as being anticipated by Foster et al., U.S. Patent 5,989,545 (hereinafter "Foster").

Claims 1-9, 12, 18-19, 26-35 have been canceled, without prejudice, in the interest of facilitating prosecution of this application. However, applicant strongly disagrees with the above-noted rejections and reserves the right to continue prosecution of claims 1-9, 12, 18-19, 26-35 at a future date.

The present pending claims 66-80 are directed to agents for treating pain comprising substance P, or substance P related compounds, such as substance P analogues, coupled to a botulinum neurotoxin.

Foster does not disclose an agent for treating pain comprising substance P, or substance P related compounds.

Therefore, Foster does not anticipate the present claims 66-80 under 35 U.S.C. 102.

Furthermore, Foster teaches that a composition for treating pain should comprise a targeting moiety which bind to the nociceptive afferents. For example, Foster indicated on column 6, lines 4-7 that:

> "According to the invention, there is provided an agent which can inhibit the release of at least one neurotransmitter... from the nociceptive afferents."

Foster does not even suggest the present invention as set forth in claims 66 to 80. Therefore, applicant submits that claims 66 to 80 are unobvious from and patentable over Foster under 35 U.S.C 103(a).

New Claims

New claims 67 to 80 are fully supported by the specification.

New claims 67 and 68 are substantially similar to canceled claims 15 and 17, respectively. Claims 15 and 17 have been rejected only under Section 112, paragraphs 1 and 2. However, as discussed above, the specification does include enabling disclosures for making and using the agent. Furthermore, the "precursor of substance P" and "substance P analogue" are clearly identified by Table 1 on pages 26-27 of the original specification. Therefore, claims 67 and 68 are fully enabled and are definite. Thus, applicant submits that claims 67 and 68 are in a condition for allowance.

New claims 69-80 seek to protect an agent comprising a toxin covalently coupled to substance P. Covalent coupling or linking of

a targeting moiety and the neurotoxin component is disclosed throughout the application. For example, page 17, lines 5-7 of the specification disclose an agent comprising a clostridial neurotoxin component or parts thereof, covalently attached or coupled to substance P. Also, the Examiner admitted that claims directed to (clostridial neurotoxin components)-(substance P) are enabled. See page 4, second sentence of the pending office action.

New claim 70 pertains to obtaining the clostridial neurotoxin component from *Clostridial beratti*, *Clostridial butyricum*, *Clostridial botulinum* and *Clostridial tetani*. This claim is fully supported by the specification. See, for example, page 15, lines 18-24.

New claim 71 refers to a botulinum toxin selected from serotypes A, B, C, D, E, F and G. This claim is fully supported by the specification. See, for example, page 15, lines 23-24.

New claim 73 seeks to protect an agent having a clostridial neurotoxin component comprising an H_N and an L chain. This claim is fully supported by the specification. For example, page 20, lines 20-24 define H_N as a fragment (about 50 kDa) derived from the H chain of a clostridial neurotoxin which is approximately equivalent to the amino end segment of the H chain, or to the portion corresponding to the amino terminal fragment in the intact H chain.

Added claims 74-76 specify that the H_N and the L chain of the clostridial neurotoxin component are taken from independent sources. This claim is fully supported by the specification. For example, page 23, lines 20-25 disclose that the H chain of a clostridial neurotoxin, in which the H_c is removed, mutated or modified, may be combined with the L-chain of a different clostridial neurotoxin, to form a hybrid.

New claim 77 is fully supported by the specification. For example, page 28, lines 6-8 disclose an agent that comprises a

clostridial neurotoxin component, for example LH_N, coupled to substance P.

New claim 78 is fully supported by the specification. For example, page 17, lines 8 though 10 disclose an agent comprising a botulinum neurotoxin toxin type A covalently coupled to substance P.

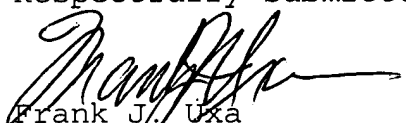
New claim 79 is fully supported by the specification. For example, page 17, lines 10-15 disclose an agent comprising botulinum toxin type A, wherein the H_c of the botulinum neurotoxin type A is removed and the remaining toxin is then covalently coupled to substance P.

New claim 80 is fully supported by the specification. For example, page 28, lines 11-13 disclose an agent where the clostridial component is a botulinum toxin type A in which the H_c has been removed or modified, coupled to substance P. See also page 22, lines 7-15.

In view of the above, applicant submits that the presently pending claims, that is claim 66 to 80, are in condition for allowance.

Applicant respectfully requests early and favorable action in the above-identified application. Should any matters remain unresolved, the Examiner is requested to call applicant's attorney at the telephone number given below.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Cancel claims 1-65, without prejudice.

Claim 66 has been amended as follows:

66. (Amended) An agent for treating pain, the agent comprising:

(a) a botulinum toxin type A proteolytic domain covalently attached to;

(b) a botulinum toxin type A translocational domain, and

(c) substance P covalently attached to the translocational domain.